#8 YC 10/22/02

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 2270**
Gordon LOWE	:	Docket No. 2001_1187A
Serial No. 09/914,264	:	Group Art Unit 1625
Filed November 30, 2001	:	Examiner R. Covington

PLATINUM (II) COMPOUNDS

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

RESPONSE

Assistant Commissioner for Patents,
Washington, D.C.

Sir:

This is in response to the Official Action dated July 16, 2002.

The claims are 1 to 7, 9 and 10.

Claims 1 to 7, 9 and 10 stand rejected under 35 U.S.C. 102(b) as being anticipated by McFadyen et al.

This rejection is untenable.

The Examiner argues that McFadyen et al teaches the complexes recited in the claims and he has referred to, in particular, page 1114.

Chart 1 on page 1114 gives different formulae for the compounds given in Table I. The compounds of relevance here are those of formula 2a to 2j and 3b. Compounds 2a to 2j are ones where the sulphur atom is linked directly to a phenyl ring whereas compound 3b is one where the sulphur atom is linked to a naphthalene ring. These compounds are not in fact covered by claim 1 since Y cannot represent an aryl group. Accordingly, it is clear that the rejection under 35 U.S.C. 102 is untenable.

If the Examiner were to reject under 35 U.S.C. 103, such rejection would also be untenable.

As stated in the first sentence of the reference, there are numerous anti-tumor agents capable of intercalative binding to DNA. The compounds disclosed are said to possess this activity.

Although Applicant's compounds are also capable of intercalating into DNA, they possess the feature which is nowhere mentioned in McFadyen et al i.e. that they act as inhibitors of thioredoxin reductase and it is believed that this is the main cause of the anti-tumor activity in Applicant's compounds. There is nothing in McFadyen et al to suggest that his compounds acted in this way.

The compounds disclosed by McFadyen et al are said to be active *in vitro* against certain tumor cells but *in vivo* they were found to be toxic. Thus it is stated at page 1115, right hand column, lines 24 to 33 that complex 2a was toxic at a dose of 5 mg/kg per day, with no mice surviving past day 9. This is in complete contrast to Applicant's compounds. Thus Table 4 on page 49 reveals that the compounds were used *in vivo* at concentrations of 50 mg/kg daily over five successive days in mice without causing any of the mice to die. This significant difference is in no way disclosed or suggested by McFadyen et al.

Applicant believes that this very different behavior *in vivo* can be attributed to the nature of the grouping attached to the sulphur atom. It is believed that thioredoxin reductase displaces the thiolate ligand from the platinum complex which thereby becomes inactivated. What this means is that the complexes of McFadyen et al will release a thiophenol or naphthalene 1-thiol which are very toxic chemicals. The compounds released by Applicant's complexes, not being phenolic, have very much lower toxicity with the result that Applicant's complexes possess a very marked advantage over the McFadyen complexes, which is in no way obvious.

Under the circumstances, it is believed that all the outstanding objections have been met and an early allowance of this application is earnestly requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact undersigned at the telephone number shown below.

Respectfully submitted,

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